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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO
09/642,405	08/21/2000	Michael P. Neeper	20413Y	8029

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EXAMINER	
LI, QIAN J	
ART UNIT	PAPER NUMBER
1632	11

DATE MAILED: 03/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No.	Applicant(s)	
	09/642,405	NEEPER ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on th c v r sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/15/02, 1/14/03* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,7,9-11,13-15 and 17-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *21-23* is/are allowed.

6)☒ Claim(s) *1-4,6,9,10,13,14,17,19,20 and 24-30* is/are rejected.

7)☒ Claim(s) *7,11,15 and 18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 August 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment filed on October 15, 2002, and January 14, 2003 has been entered and assigned as Paper Nos. 8 and 10. Claims 5, 8, 12, and 16 have been canceled, claims 1, 6, 9, 10, 13, 14, 17, 19, 21-26, 28, and 30 have been amended, and claims 1-4, 6, 7, 9-11, 13-15, 17-30 are pending and under current examination.

The arguments in paper No. 8 which have been rendered moot in view of the amendment of claims and modification of the rejections will not be further addressed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

WRITTEN DESCRIPTION REQUIREMENT

Claims 1-4, 6, 9, 10, 13, 14, 17, 19, 20, and 24-30 stand rejected under 35 U.S.C. 112, first paragraph, and the rejection has been modified in view of the amendment to claims.

The amended claims recite, "a synthetic polynucleotide comprising a sequence encoding a codon-optimized HPV16 protein, or mutated form thereof which has reduced protein function for viral replication and cellular transformation". Given the broadest reasonable interpretation, the claims read on a) further mutating the codon optimized HPV16 polynucleotide sequences; or b) a sequence encoding a mutated HPV16 protein having a particular function.

In paper #8, applicants argue that the specification defines "synthetic", teaches how to modify cordons so that they are preferred for human expression, and provides numerous examples directed to four proteins and three HPV serotypes, applicants were in possession of the claimed invention.

In response, although the specification teaches how to optimize a codon for HPV16 to enhance the expression of HPV16 proteins in human cells, it is silent with regard to further mutate the codon-optimized sequences, or mutated HPV16 proteins; it fails to define the term for mutant HPV16 proteins, whether they encompass other serotype of HPV proteins or another type of HPV16 proteins. Particularly, since the claims embrace a mutated protein at any length having any modification, the specification fails to teach which mutant of HPV16 protein maintains the function for viral replication and cellular transformation as compared to a wild-type protein. Accordingly, the specification fails to support the full scope of the claims.

For reasons of record and those set forth above, the instant specification fails to meet the written description requirement set forth under 35 U.S.C. §112, 1st paragraph.

ENABLEMENT REQUIREMENT

To the extent that the claimed subject matter is not sufficiently described in the instant disclosure, claims 1-4, 6, 9, 10, 13, 14, 17, 19, 20, and 24-30 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention,

since a disclosure cannot teach one to make or use something that has not been described.

The rejection of claims 24-29 under 35 U.S.C. 112, first paragraph has been modified in view of the amendment to claims, because the specification, while being enabling for inducing an immune response to HPV16 infection in a subject using a polynucleotide encoding a codon-optimized HPV16 protein by intramuscular injection of the polynucleotide, does not reasonably provide enablement for inducing a protective immune response to *any* serotype HPV infection in a subject using a polynucleotide encoding a codon-optimized HPV16 protein by *any* route of administration. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The amended claims limit the polynucleotide vaccine to encoding a codon-optimized HPV16 protein, however, the preamble of the claims are drawn to inducing immune responses to any human papillomavirus including any serotype of HPV. The specification is silent with regard to whether different serotypes of HPV crossreact, and the art of record teaches that various HPV types do not crossreact with regard to the induction of both humoral and cell-mediated immunity (Bubenik, J, Int. J. Oncol 2002;20:207, abstract). In view of such, the invention does not appear to be enabled in the absence of clarification of the contradictory evidence found in the reference.

The amended claims recite administering to a vertebrate subject a polynucleotide encoding a codon-optimized HPV16 protein. Given the broadest reasonable interpretation, the claimed methods embrace any route of administration, such as subcutaneous, intravenous, and intraperitoneal injection. However, the only means of administration taught by the specification is intramuscular injection. In view of the state of the art regarding routes of genetic vaccination, *McCluskie et al* (Mol Med 1999 May;5:287-300) teach "ROUTES OF ADMINISTRATION OF PLASMID DNA VACCINES INFLUENCES THE STRENGTH AND NATURE OF IMMUNE RESPONSES IN MICE AND NON-HUMAN PRIMATES" (See abstract). *Nakano et al* (J Virol 1997;71:7101-09) teach that immune reactivity with plasmid DNA encoding HCV-E2 antigenic domains is linked to the injection mode, "DIFFERENT ROUTES OF INJECTION OF HCV E2 PLASMID CAN RESULT IN QUANTITATIVELY AND QUALITATIVELY DIFFERENT HUMORAL IMMUNE RESPONSES" (see abstract). The specification fails to teach whether the claimed method could induce an immune response in a subject by any route of administration, thus, fails to provide an enabling disclosure commensurate with the scope of the claims.

Therefore, in view of the limited guidance, the lack of predictability of the art and the breadth of the claims, one skill in the art could not practice the invention without undue experimentation as it is broadly claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 6, 9, 10, 13, 14, 17, 19, 20, and 24-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are vague and indefinite because the amended claims recite, "a synthetic polynucleotide comprising a sequence encoding a codon-optimized HPV16 protein, or mutated form thereof". The claim language read on a) further mutating the codon optimized HPV16 polynucleotide sequences; or b) a sequence encoding a mutated HPV16 protein. It is unclear what applicants intent to claim, thus, the metes and bounds of the claims are unclear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Previous rejection of claims 1-6, 22, and 30 under 35 U.S.C. 102(e) as being anticipated by *Hofmann et al* (US 6,159,729) is withdrawn in view of the amendment to claims.

Previous rejection of claims 1-5, 22, and 30 under 35 U.S.C. 102(e) as being anticipated by *Joyce et al* (US 5,820,870) is withdrawn in view of the amendment to claims.

Previous rejection of claims 1-6, 8-10, 12, 13, 16, 17, 22, and 30 under 35 U.S.C. 102(e) as being anticipated by *Whittle et al* (US 6,123,948) is withdrawn in view of the amendment to claims.

Previous rejection of claims 1-6, 19, 20, 21, and 26 under 35 U.S.C. 102(e) as being anticipated by *Ertl et al* (US 6,019,978) is withdrawn in view of the amendment to claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Previous rejection of claims 1-6, 8-10, 12, 13, 16, 17, 19-26, 28, and 30 under 35 U.S.C. 103(a) as being unpatentable over *Ertl et al* ((US 6,019,978) as applied to claims 1-6, 19, 20, 21, and 26 above, and *Whittle et al* (US 6,123,948) as applied to claims 1-6, 8-10, 12, 13, 16, 17, 22, and 30, and further in view of *Donnelly et al* (J Infect Diseases 1996;713:314-20) is withdrawn in view of the amendment to claims.

Claim Objections

Claims 7, 11, 15, and 18 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Claims 21-23 are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).

Q. Janice Li
Examiner
Art Unit 1632

QJL
March 18, 2003

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER